immunizations 411

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webinar series

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Travel Vaccines

15 June 2017

Disclosures

- Wilbur Chen received research grants from PaxVax, Inc. as the Principal Investigator for the pivotal licensure studies of Vaxchora
- PaxVax, Inc. is the manufacturer of Vivotif and Vaxchora

Webinar Objectives

- Highlight 6 common travel vaccines
- Understand the geographic locations or epidemiology of the 6 vaccine preventable diseases
- Become familiar with the current vaccine recommendations for these travel vaccines

- *Unable to review all possible travel vaccines*
- *Unable to review issues in preventing travel-related illnesses (i.e., traveler's diarrhea, malaria, mosquito prevention, altitude sickness, etc.)*
- *Unable to discuss medical evacuation, travel insurance, or other possible travel medicine matters*

Protection during travel

High-Risk Activity…High-Risk for Infection!

Licensed Travel Vaccines in U.S.

- Yellow Fever
- Typhoid
- Hepatitis A
- Japanese Encephalitis
- Cholera
- Meningococcal
- Rabies
- Poliovirus
- Influenza
- Tetanus
- Measles, Mumps, Rubella
- Hepatitis B
- Pneumococcal
- Varicella
- ~~Tick-borne encephalitis~~
- ~~Anthrax~~
- ~~Smallpox~~
- ~~Tularemia~~

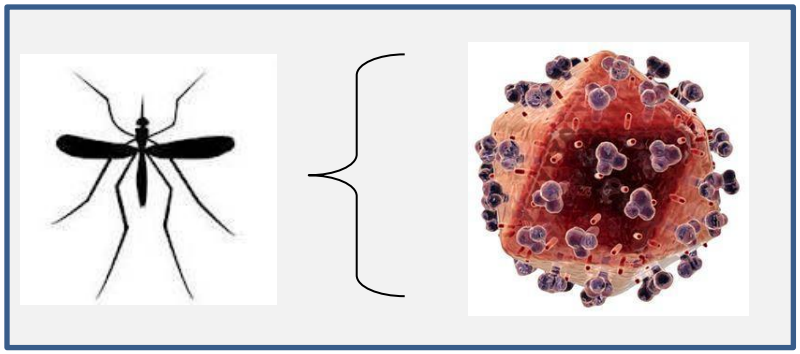
Organization of Lecture

- Pathogen
- Epidemiology/Geography
- Clinical Presentation
- Risk Assessment & Preventive Measures
- Vaccine(s) Available
  - Contraindications/Precautions
  - Adverse Effects
  - Efficacy

Beware of insect bites…

Yellow Fever

- Caused by a Flavivirus
- Transmitted by mosquito bite (*Ae. aegypti*)
- YF causes 200,000 cases of clinical disease and 30,000 deaths each year[1]
- Substantial underreporting[2], due to rural nature



1. WHO. Yellow Fever fact sheet, no. 100
2. Weekly Epi Rec 1990; 65: 213

YF: Epidemiology

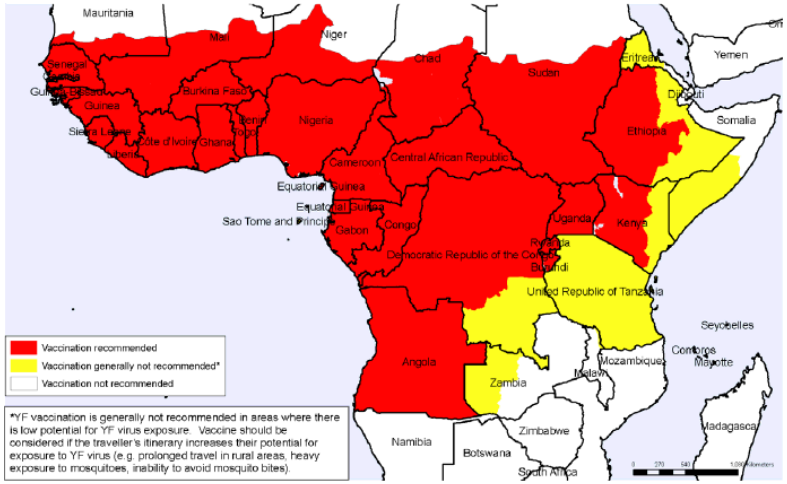
Geography

Sub-Saharan Africa

- 87% cases and 50% case-fatality ratio

Tropical South America

- 13% cases and 20% case-fatality ratio



Seasonality

- All-year but peaks with mosquito breeding
- **South America**: peak rainfall, humidity, temp = Jan-May
- **West Africa**: late rainy season to early dry season = July-Oct

WHO YF Risk Maps, Feb 2011

YF: Clinical Presentation

- Majority of human infections are asymptomatic
- But, spectrum can be mild to severe

- Incubation 3-6 days
- Initial stage: Abrupt Fever and severe Headache; non-specific flu symptoms
- Recovery period or brief remission (viremia present): 1 day
- Toxic phase (15%): F, N/V, myalgia, arthralgia, jaundice epigastric pain, renal insufficiency, and cardiovascular instability (viremia often not present)
  - Multi-organ failure with bleeding diathesis.
  - Case-fatality ratio 20-50%; especially with severe yellow fever with hepatorenal dysfunction

YF: Risk to Traveler

2-week stay for unvaccinated traveler:

- West Africa 50 illnesses per 100,000
- South America 5 illnesses per 100,000

YF: Prevention

- Clothing barrier
- Insect repellent (DEET)
- Vaccination

There is no specific treatment, limited to supportive care

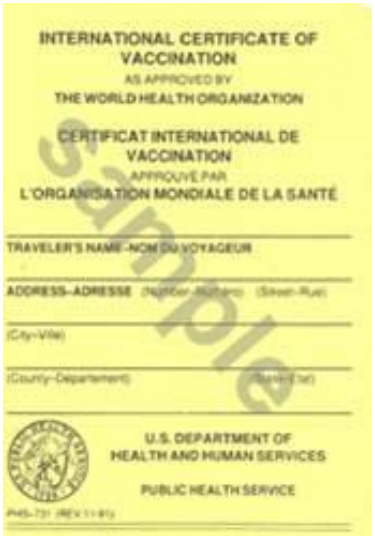
Globally available YF Vaccines

Manufacturer:	WHO pre-qualify:
• Sanofi Pasteur, France	1987
• Institut Pasteur de Dakar, Senegal	1999
• Bio-Manguinhos, Brazil	2001
• FSUE Chumakov, Russia	2009

YF Vaccine available in U.S.

YF-Vax® (sanofi pasteur)

- Live, attenuated 17D-204 strain
- Single parenteral dose, 0.5 mL
- Approved: age ≥9 months
- International Certificate of Vaccination
  - valid beginning 10 days after the date of vaccination



International Health Regulations (IHR), since June 2016

- *WHO World Health Assembly in May 2014: lifetime (i.e., no booster doses necessary).*

ACIP recommendations (Feb 26, 2015)

- *10 year boosters not required*

…Availability of YF Vaccine

SANOFI PASTEUR

April 2017

Dear Health Care Professional:

This letter is to provide an update on the status of YF-VAX® (Yellow Fever Vaccine) supply. Sanofi Pasteur is experiencing delays in the production process of YF-VAX vaccine and it is anticipated that the product will be unavailable from mid-2017 to mid-2018 as we transition production to a new state-of-the-art facility. Ordering restrictions have been implemented to responsibly manage the limited remaining supply of YF-VAX vaccine. YF-VAX vaccine will continue to be available while current supplies last.

Once YF-VAX vaccine is no longer available, health care providers and patients will be able to find locations that will administer STAMARIL vaccine by visiting the CDC web page at http://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search. They may also visit http://wwwnc.cdc.gov/travel/ for information about which countries require yellow fever vaccination for entry and for which countries the CDC recommends yellow fever vaccination.

YF Vaccine: Contraindications

- Hypersensitivity to vaccine components: egg/chicken proteins, gelatin, latex (vial stopper)
- Prior anaphylaxis with vaccination
- Immunedeficiencies

  symptomatic HIV, CD4 <200, malignant neoplasms, transplantation, etc.
- Infants age <6 months

YF Vaccine: Precautions

- Age 6-8 months or Age ≥60 years
- Pregnancy and breastfeeding
- Asymptomatic HIV and CD4 200-499

YF Vaccine: Safety and Adverse Effects

- 10-30% mild systemic reactions

  low-grade fever, headache, myalgia

- Hypersensitivity

  1.8 cases/100,000 doses

- Vaccine-associated Neurologic Disease (YEL-AND)

  3-28 d post-vax: Meningoencephalitis, GBS, bulbar/Bell palsy

Overall:	0.8 cases/100,000 doses
Age 60-69:	1.6 cases/100,000 doses
Age ≥70:	2.3 cases/100,000 doses

- Vaccine-associated Viscerotropic Disease (YEL-AVD)

  Viremia w/multi-organ involvement (63% case fatality)

Overall:	0.4 cases/100,000 doses
Age 60-69:	1.0 cases/100,000 doses
Age≥70:	2.3 cases/100,000 doses

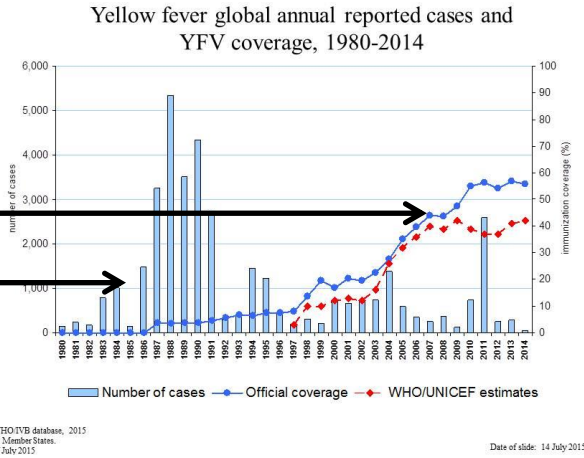
YF Vaccine: Protection

In endemic populations (assuming vaccine coverage of 60-80% of population):

Within 10 d	80-100% immunity
After 30 d	≥99% immunity[1]

Vaccine Coverage

Case Count



Among vaccinated travelers from industrialized countries: One case, non-fatal (Spain to West Africa, 1988)[2]

1. MMWR 2010; 59: 1-27 & Vaccines, 5th ed: 2008: 959
2. Lancet 1989: 334:1275

Fig. WHO 2015

YF Outbreak: Angola

(12/2015-7/2016)

Yellow Fever outbreak in Angola

- 3818 suspected cases
- 879 lab-confirmed infections
- 369 deaths
- Exported cases:
  - Dem Rep Congo, n=74
  - Kenya, n=2
  - China, n=11
- YF mass vaccination campaign (initiated 2/2/16)
  - 18 million doses (by mid-June 2016)

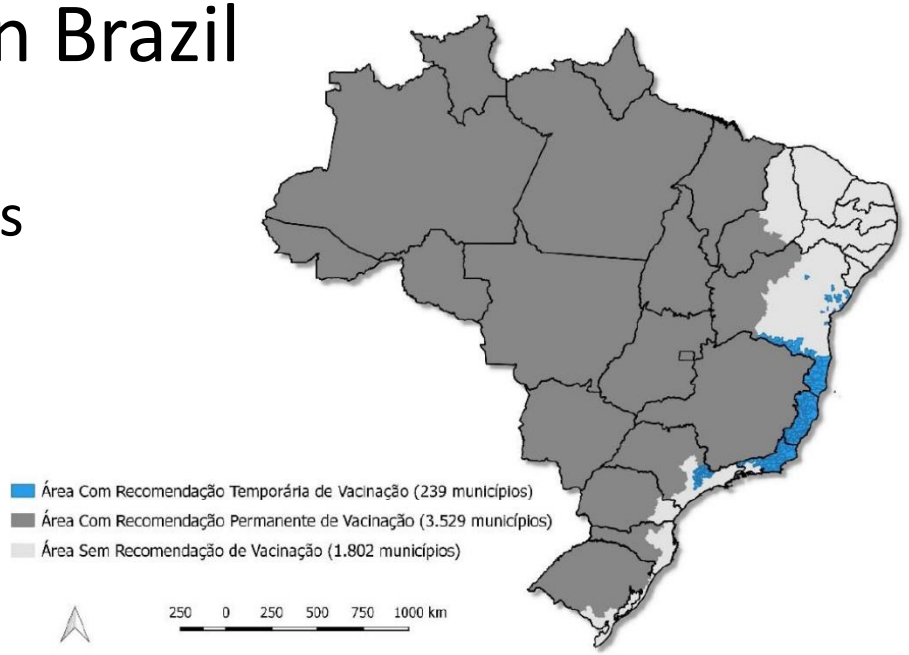
China:
Of 5 with vaccination status info, all 5 cases did not have YF vaccine

YF Outbreak: Brazil

(12/2016-ongoing)

Yellow Fever outbreak in Brazil

- ~2900 suspected cases
- 681 lab-confirmed infections
- 372 deaths



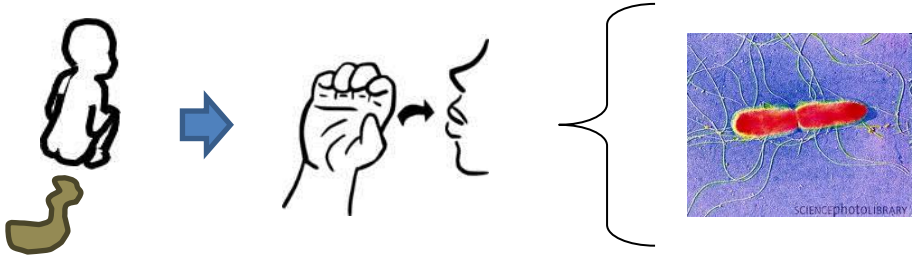
- YF mass vaccination campaign
  - 67 million doses

Ministry of Health, Brazil
CIDRAP update, 20 Apr 2017

Beware of risk through ingestion…

Typhoid

- Human host-restricted bacterial pathogen
- *Salmonella enterica* subspecies *enterica* serovar Typhi (*S*. Typhi)
  - *S*. Typhi: 22M illnesses and 200,000 deaths per year
- serovars Paratyphi A, B, or C (*S*. Paratyphi).
  - *S*. Paratyphi: 6M illnesses
- ❖ Nontyphoidal *Salmonella* (NTS) include: *S*. Enteriditis and *S*. Typhimurium
- Transmission: fecal-oral



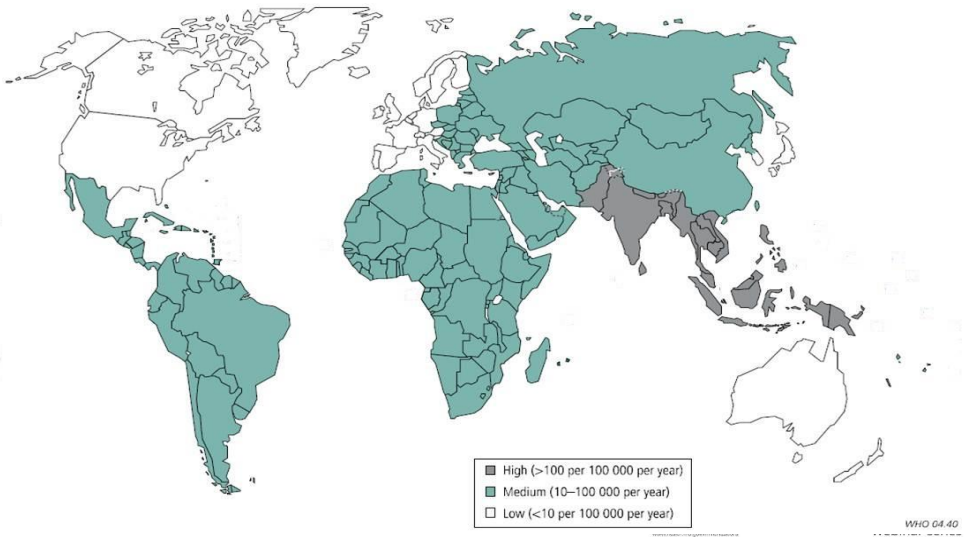
Bull WHO 2004; 82:346-353

Typhoid: Epidemiology

- Associated with poor sanitation and lack of access to clean water
- World-wide distribution

High Incidence	>100 cases / 100,000 person years
Medium	10-100 cases / 100,000 person years

- Highest risk: Southern Asia (6-30x higher than other regions
- No seasonality



Bull WHO 2004; 82:346-353

Typhoid: Clinical Presentation

- Incubation 6-30 days
- Insidious Onset: gradual fatigue and fevers (102-104°F); abdominal pain, headache, malaise, anorexia, chills
- Without therapy: illness duration 3-4 weeks
- Classic Presentation:

  1st week - *stepwise* fever w/ bradycardia (pulse-temp dissociation)

  2nd week - abdominal pain and "rose spots"

  3rd week – hepatosplenomegaly, intestinal bleeding, perforation

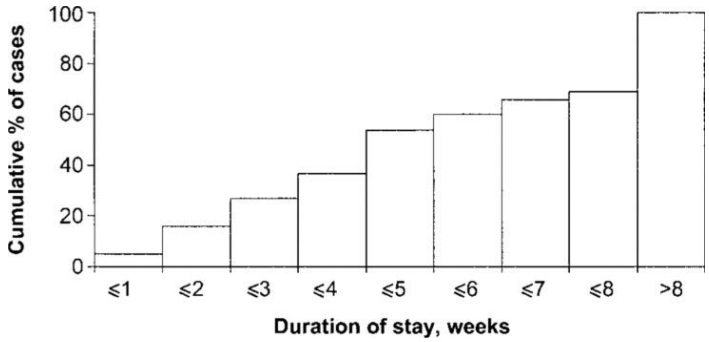
- 15% serious complications: Intestinal hemorrhage, perforation, peritonitis, septic shock
- Chronic Carrier State: 1-6% infections; excrete organisms >1 year

  More common in women and those with cholelithiasis or abnormal biliary tract

Typhoid: Risk to Traveler

CDC data, all travelers during 1994-1999:[1]

- 1027 typhoid cases, 3 deaths
- –Risk associated with length of stay
- –Risk associated with location
  - 53% Indian subcontinent
  - 17% Mexico/Central America
  - 7% Caribbean
  - 3% Africa
  - 4% other



CDC data, travelers to SE Asia during 2008-2011:[2]

- 602 typhoid and 142 paratyphoid A cases
- 5% typhoid cases and 20% paratyphoid cases were vaccinated

1. CID 2004; 39: 186-91
2. Vaccine 2014; 32: 3577-9

Typhoid: Prevention & Treatment

Prevention:

- Safe food and water
- Vaccination

Treatment:

- Rehydration
- Prompt Antibiotics
  - First Line: Fluoroquinolones, 3rd Gen Cephalosporin, azithromycin
  - Beware: FQ resistance in SE Asia!
- Surgery - ileal perforation
- corticosteroids

Globally Available Typhoid Vaccines

Parenteral vaccine:

- Typhoid Vi capsular polysaccharide
  - Typherix (GSK), Typhim Vi (SP), TypBar (Bharat), Shantyph (Shanta), Typho-Vi (BioMed), Zerotyph (Boryung, S. Korea), Typhevac (Shanghai)
- Typhoid Vi conjugate (TT)
  - Peda-typh (BioMed, India), Typbar-TCV (Bharat)
- Combination: ViCPS+Hepatitis A
  - Hepatyrix (GSK), Vivaxim (SP)

Oral vaccine:

- Live Attenuated
  - Vivotif (PaxVax)

Typhoid Vaccines available in the U.S.

Typhim Vi® (sanofi pasteur)

- Purified Vi capsular polysaccharide (Vi PS)
- Single parenteral dose, 0.5 mL
- Approved: age ≥2 years
- Booster every 2-3 years

Vivotif® (Crucell-PaxVax)

- Live, attenuated bacterial strain (Ty21a)
- 4 oral doses, spaced alternating days
- Approved: age ≥6 years
- Booster every 5-6 years

Typhoid Vaccine: Contraindication/Precautions

Typhim Vi®

- Hypersensitivity to vaccine components: typhoid polysaccharide, phenol, PBS
- Prior anaphylaxis with vaccination

Delay for concurrent acute febrile illness

Vivotif®

- Hypersensitivity to vaccine components:
- Prior anaphylaxis with vaccination
- Immunedeficiencies

Delay for concurrent acute febrile illness

Efficacy reduced with concurrent antibiotics

Typhoid Vaccine: Safety & Adverse Effects

Typhim Vi®

70-77%	injection site pain, mild
42%	headache
35%	fatigue
1%	fever

Vivotif®

6%	abdominal pain
6%	nausea
5%	headache
3%	fever
3%	diarrhea
<2%	vomiting
1%	skin rash

No transmission recorded

No vaccinemia or reversion events reported

Typhoid Vaccine: Protection

Typhim Vi®

- Nepal field trial (1986-88):[1]
  75% protection against typhoid fever
- South Africa field trial (1985-88):[2]
  55% protection against typhoid fever
- India field trial (2004-6): [3]
  61% protection

Meta-Analysis (2007): [4]

55% cumulative efficacy at 3 years

Vivotif®

- Egypt field trial (1978-81):[5]
  96% protection
- Chile field trials (1982-87):
  59% protection, two-doses[6]
  67% protection, three-doses[7]
- Indonesia field trial (1986-89):
  79% protection, three-doses[8]

Meta-Analysis (2007): [4]

51% cumulative efficacy at 3 years

Protection in U.S. travelers using either vaccine (2008-11):[9]
80% vaccine efficacy

1. NEJM 1987; 317: 1101-4
2. Lancet 1987; 2:1165-9
3. NEJM 2009; 361: 335-44
4. Vaccine 2007; 25: 7848-57
5. JID 1982; 145: 292-5
6. Vaccine 1990; 8: 81-4
7. Lancet 1987; 1: 1049-52
8. Lancet 1991; 338: 1055–9
9. Vaccine 2014; 32: 3577-9

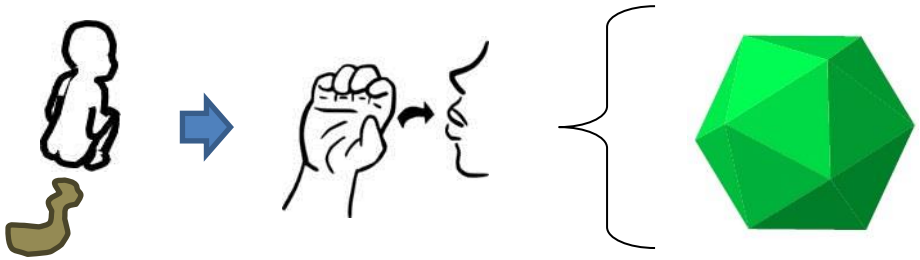
Typhoid Vaccine covers these agents of "Enteric Fever"

- Typhoid
- ~~Paratyphoid (*S*. Paratyphi A, B, and C)~~
- ~~Non-typhoidal *Salmonella*~~
  - ~~*S*. Enteritidis~~
  - ~~*S*. Typhimurium~~
  - ~~*S*. Dublin~~
  - ~~*S*. Choleraesuis~~
  - ~~*S*. Heidelberg~~
  - ~~*S*. Newport~~
  - ~~*Others*…~~

Beware of additional risk through ingestion…

Hepatitis A

- Positive-stranded RNA virus
  - *Picornaviridae* family, *Heparnavirus* genus
- Primarily human host-restricted pathogen
  - Some non-human primate sp. hosts
- Single serotype
  - 4 genotypes, but not important for biology
- Transmission: fecal-oral

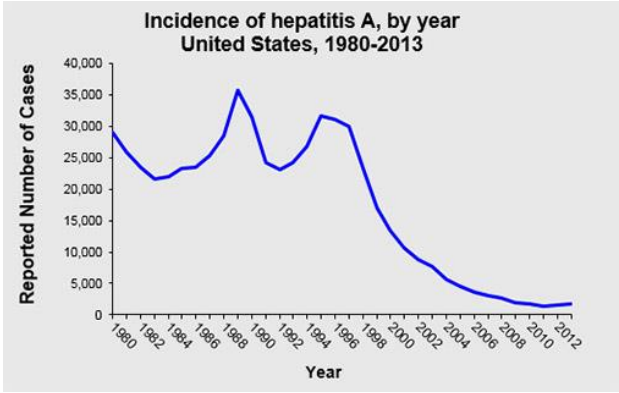


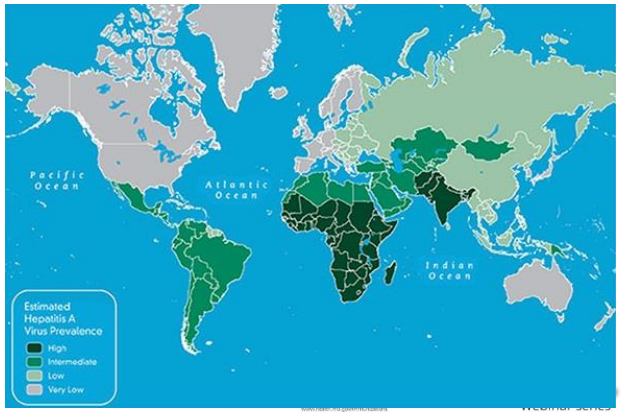
HAV: Epidemiology

- Associated with poor sanitation and hygiene
- Decline in U.S. with vaccination
- World-wide distribution
- Highest risk:

  Sub-Saharan Africa, South Asia
- Intermediate risk:

  Central & South America
- No seasonality





CDC Statistics & Surveillance
CDC 2005 data

HAV: Clinical Presentation

- Incubation period: average 28 days (range 15-50 days)
- Age <6 years: majority asymptomatic, 10% jaundice
- Older than 6 yrs: >70% jaundice
- Abrupt Clinical Illness:
  - Fever, fatigue, loss of appetite, nausea, vomiting, joint pain, abdominal pain, dark urine, clay-color stools, jaundice
- Duration: usually 2 months, 10-15% prolonged/relapsing up to 6 months
- Case-Fatality: Overall 0.3% (1.8% for age >50 yrs)

HAV: Risk to Traveler

- CDC, estimated HAV cases (endemic and travelers):[1]
  - 2011 - 2700 cases
  - 2012 - 3000 cases
  - 2013 - 3500 cases
- Swedish travelers (1997-2005),[2]
  - 636 travel-related cases
  - East Africa, 14.1 cases /100,000 person months
  - Middle East, 5.8 cases /100,000 person months
  - Indian subcontinent, 5.6 cases/ 100,000 person months
  - Risk highest among those Visiting Friends & Relatives (VFR)
- Dutch travelers (2003-2011),[3]
  - 2094 total cases, 931 (44%) from travel
  - Attack rate during 2003-2005, 7.5 per 100,000 travelers
  - Attack rate during 2009-2011, 3.5 per 100,000 travelers

1. CDC Statistics & Surveillance 2. J Travel Med 2009; 16:233-8 3. J Travel Med 2015; 22: 208-11

Globally Available HAV Vaccines

Inactivated vaccines:

- Monovalent
  - Avaxim (SP), Havrix (GSK), Vaqta (CSL/Merck)
- Combination: HAV+ViCPS
  - Hepatyrix (GSK), Vivaxim (SP)
- Combination: HAV+HBV
  - Twinrix (GSK)

Live Attenuated vaccine:

- H2 & L-A-1 strains (China)

HAV Vaccines available in U.S.

Havrix® (GSK)

- inactivated
- Approved since 1995

Adults:
1 mL IM at 0 & 6-12 m

Children (1-18 y):
0.5 mL IM at 0 & 6-12 m

Vaqta® (Merck)

- inactivated
- Approved since 1996

Adults:
1 mL IM at 0 & 6-18 m

Children (1-18 y):
0.5 mL IM at 0 & 6-18 m

Combined A/B

Twinrix® (GSK)

- inactivated
- Approved since 2001

Adults: 1 mL IM

Children: not "approved"

Standard Dosing:
0, 1, 6 m

Accelerated: Dosing:
0, 7, 21-30d; 12 m

Since 2006, routine vaccination of children age ≥1 year*

* MMWR 2006; 55: RR-7

HAV Vaccines:
Contraindications/Precautions

- Prior anaphylaxis with vaccination
- Hypersensitivity to a vaccine component: viral antigen, aluminum hydroxide adjuvant, neomycin
- Latex, vial stopper and syringe plunger
- No special precautions for the immunocompromised

HAV Vaccines:
Safety & Adverse Effects

Adults:

- Injection site soreness (56%)
- Headache (14%)
- Malaise (7%)

Children:

- Injection site soreness (15%)
- Feeding problems (8%)
- Headache (4%)
- Injection site induration (4%)

HAV Vaccines: Protection

- Protective antibodies:[1]
  - First dose, ≥94% adults and ≥97% children
  - Second dose, 100% adults and children
- Havrix® Thailand field trial:[2]
  - Efficacy 94% (CI 79-99%) after 2 doses, 1 m apart
- Vaqta® New York trial:[3]
  - Efficacy 100% (CI 87-100%) after 1 dose

1. MMWR 2006; 55: RR-7
2. JAMA 1994; 271: 1328-34
3. NEJM 1992; 327: 453-7

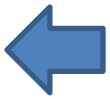
HAV Vaccines:
"Off Schedule"

Delayed second dose:

- Adults, Two-dose, 18 months apart: 100% protective antibody after second dose[1]
- Children, Two-dose, 4-8 years apart: 100% protective antibody after second dose[2]

1. Vaccine 2003; 21: 3208-11
2. J Travel Med 2004; 11:120-1

Which of the following is not a Flavivirus?

A. Chikungunya 

B. Dengue

C. Tick-borne Encephalitis

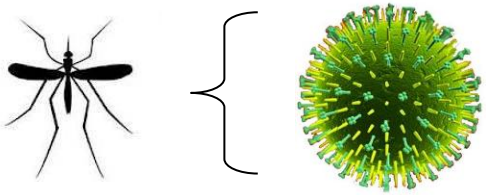
D. West Nile

E. Yellow Fever

F. Zika

Japanese Encephalitis

- Caused by a Flavivirus
- Transmitted by mosquito bite (*Culex* sp.)
- JE is estimated to cause ~68,000 clinical cases each year[1]
- Most important cause of viral encephalitis in Asia and Western Pacific
- Substantial underreporting[2], due to rural nature



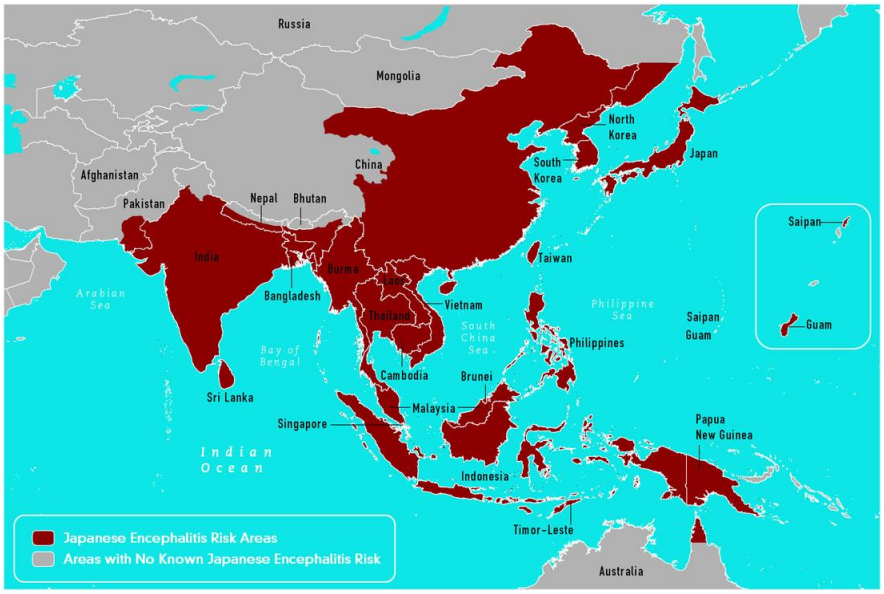
1. Bull WHO 2011; 89:766-74
2. Vaccine 2000; 18: 1-25

JE: Epidemiology

Geography

Asia & Western Pacific

- Rural agricultural areas (e.g., rice farming)
- 20-30% case-fatality ratio



Seasonality

- Temperate: peaks summer and fall
- Tropics: all year with peaks during rainy (monsoon) season

JE: Clinical Presentation

- <1% of JE infection develop clinical illness
- ~1 in 200 infections result in severe disease

- Incubation 5-15 days
- Initial stage: Fever, Headache, Vomiting
- Progression to Severe disease (days): **encephalitis**, mental status changes, neurological symptoms, movement disorders, seizures (children especially), or death

- Among those with encephalitis, 20-30% fatality
- Among those recovering from acute illness, 30-50% survivors have residual neurologic, cognitive, or psychiatric symptoms

JE: Risk and Prevention

Risk

- Endemic incidence, 1.8 cases per 100,000 residents
- Estimated incidence among unvaccinated travelers to Asia <1 case per 1 million travelers
- 7 documented US traveler cases (1973-2011)

Prevention

- Clothing barrier
- Insect repellent (DEET)
- Vaccination
  - There is no specific treatment, limited to supportive care

Bull WHO 2011; 89:766-74
CDC Yellow Book 2014

Globally Available JE Vaccines

Inactivated vaccine:

- Vero cell, alum-adjuvanted (Intercell) – N. America, Australia, Europe
- Vero cell (Beijing-1 strain) - Japan

Live Attenuated vaccine (Chengdu Inst. Biol Products):

- SA_{14}-14-2 strain - China, India, Nepal, Korea, Sri Lanka, Thailand

Live Chimeric vaccine (SP):

- YF 17D backbone - Australia & Thailand

JE Vaccine in US

Ixiaro® (Intercell)

- Inactivated, whole-virus
- Vero cell culture-derived
- SA_{14}-14-2 attenuated strain
- Approved (2009):

  Age ≥3 years
  Two parenteral doses, 0.5 mL, spaced 28 days

  Age 2 months to <3 years
  Two parenteral doses, 0.25 mL, spaced 28 days

  Booster dose after 1 year

**JE-Vax (inactivated mouse brain-derived vaccine) is no longer produced, expired May 2011*

JE Vaccine

Contraindications

- Severe Allergic Reactions to vaccine components: protamine sulfate
- Prior anaphylaxis with vaccination

Precautions

- Hypersensitivity to vaccine components
- Immunocompromised may have diminished protection

JE Vaccine: Adverse Effects

Adults:

- Injection site pain (25%)
- Headache (20%)
- Myalgia (10%)

Better tolerated than JE-Vax

Children (1-3 years):

- Fever (20%)

Infants (1-11 months):

- Injection site redness (15%)
- Fever (20%)
- Irritability (15%)
- Diarrhea (10%)

JE Vaccine: Protection

- Thailand field trial of JE-MB[1]
  - Efficacy 91%
- Taiwan, trial of JE-MB, 30-years experience
  - Efficacy 97%[2]
  - Incidence 1967 (pre-vaccination), 2.05 cases per 100,000[3]
  - Incidence 2003, 0.11 cases per 100,000[4]
- Neutralizing antibody ($PRNT_{50}$) of ≥1:10 is a reasonable surrogate of protection[5]

1. NEJM 1988; 319: 608-14
2. Vaccine 2006; 24: 2669-73
3. AJTMH 1999; 61: 78-84
4. Epi Rev 1999; 21: 73-86
5. FDA, 16 May 2013 and Vaccine 2005; 23: 5205-11

"Off Label"
JE Vaccine: Accelerated Schedule

- Vaccination should be completed at least 1 week prior to potential exposure
- JE Accelerated Schedule: phase 3 study of Ixiaro and rabies[1]
  - Day 1 (JE/Rab), Day 4 (Rab), Day 8 (JE/Rab)
  - Non-inferior, rapid short-term protection for up to 2 months

    99% seroprotection in accelerated schedule

    100% seroprotection in routine schedule

J Travel Med 2015; 22: 225-31

JE Vaccine: Booster Doses

JE Booster Doses

- Current recommendation: single booster at 12-24 months
- 76 months (6.3 years) after booster dose, 96% (64 of 67) maintained PRNT Ab

Vaccine 2015; 33: 3600-04

Beware of sewage contamination of your water…

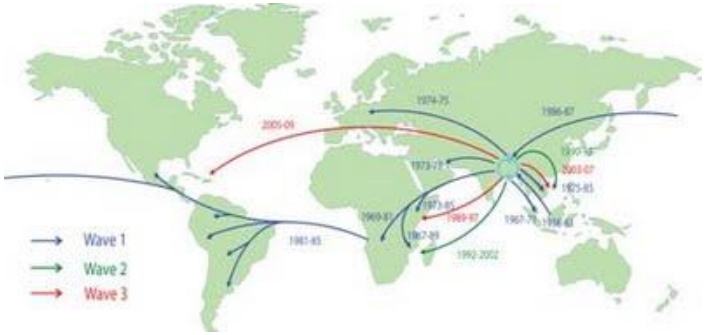
Cholera

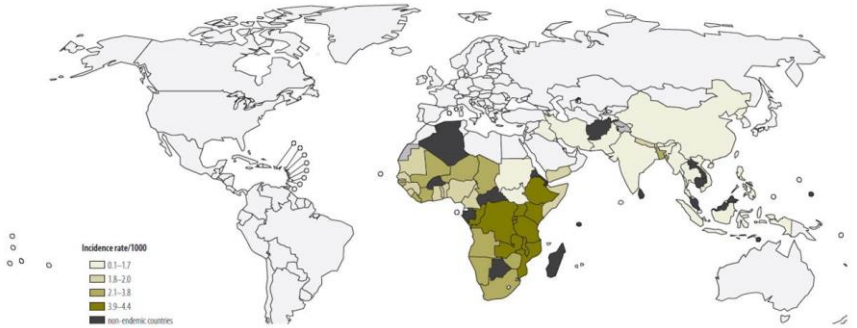
- *Vibrio cholerae*
- Serogroups O1 (and O139)
  - Serotype Inaba or Ogawa
  - Biotype El Tor or Classical
- Rapidly dehydrating diarrhea
- 1.4-4.3 million cases and 28,000-142,000 deaths annually[1]
- Transmission: fecal-oral

WHO, July 2015

Cholera Epidemiology

- Pandemics
  - Currently 7th (since 1961)
- Epidemics
  - *Example*: post-earthquake Haiti in 2010
- Endemic
  - *Examples*: India, Nigeria, DRC, Tanzania, Kenya, Ethiopia, Bangladesh





Ali, Bull WHO 2012; 90:209

Globally Available Cholera Vaccines

- Oral inactivated monovalent
  - Dukoral (Crucell)
- Oral inactivated bivalent
  - Shanchol (Shantha)
  - Euvichol (EuBiologics)
- Oral, live monovalent
  - Vaxchora (PaxVax)

Cholera Vaccine in U.S.

Vaxchora (PaxVax)

- Live, attenuated O1 classical Inaba strain (CVD 103-HgR
- Single-dose
- Approved age 18-64 years
- Licensed June 10, 2016
- ACIP Recommendation (June 22, 2016)[1]

  "Cholera vaccine (CVD 103-HgR, Vaxchora™) is recommended for adult (18-64 years old) travelers to an area of active cholera transmission"

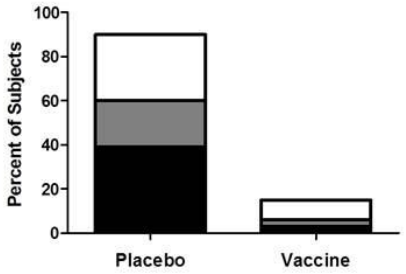
MMWR , Vol 66, No 18, 12 May 2017

Cholera Vaccine: Protection

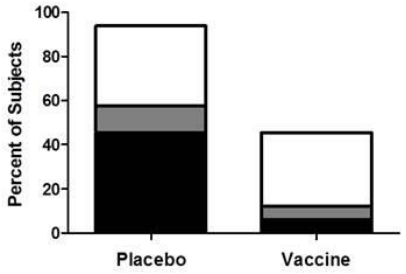
Primary Efficacy (Mod-Severe Diarrhea)

	Vaccine 10-Day	Vaccine 3-Month
Vaccine Efficacy	**90.3%**	**79.5%**
95% CI	62.7-100	49.9-100

10 Day Challenge

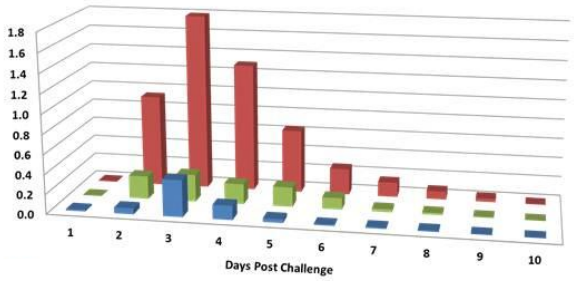


3 Month Challenge

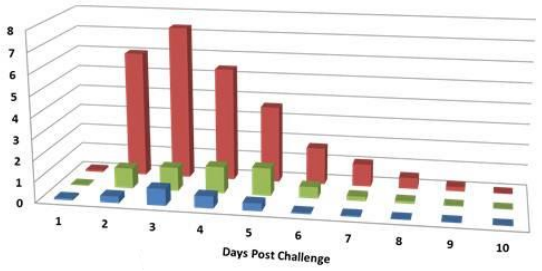


Mild Diarrhea
Moderate Diarrhea
Severe Diarrhea

Average Volume of Diarrhea



Average No. of Diarrheal Stools



10-Day Vaccinee n=35
3-Month Vaccinee n=33
Combined placebos n=66

Chen, CID 2016

Cholera: High Risk Populations

Risk of Infection:

- Travelers visiting friends and relatives
- Long-term travelers (e.g., expatriates)
- Travelers who do no follow safe food and water precautions and personal hygiene (e.g., adventure backpacking)
- Healthcare, aid, relief, and response workers with direct contact with cholera patients

Risk of Poor Outcome with cholera:

- Travelers without ready access to rehydration therapy and medical care
- Blood type O
- Pregnant
- Immunocompromised
- Chronic cardiovascular or renal disease

Meningococcal Meningitis

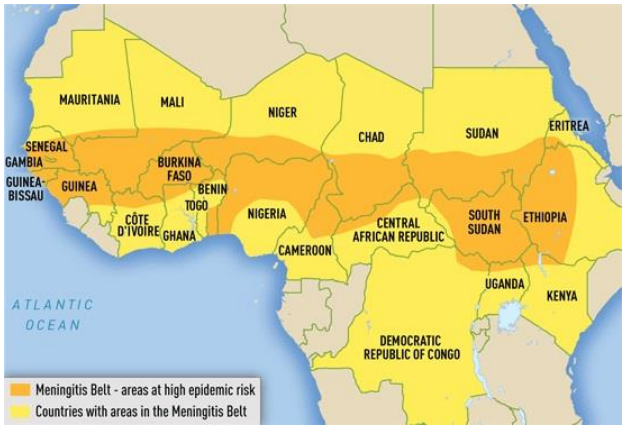
- *Neisseria meningitidis*
- 6 major serogroups: A, B, C, W-135, X, and Y
- Incidence: (cases/100,000 population)
  - Americas, Europe, Australia 0.3-3/100K
  - Sub-Saharan Africa 100-1000/100K

"Meningitis Belt"

Dry season (Dec – June)

5-10% of population are carriers

Serogroup A,C,X,W



CDC Yellow Book 2016

Meningococcal Vaccines in the U.S.

Monovalent, group B (Bexsero, Trumenba)

Combination

- C, Y, Hib-TT (MenHibrix)

Quadrivalent Polysaccharide (Menomune)

Quadrivalent Conjugate (Menactra, Menveo)

Meningococcal Vaccines for Travel

To Saudi Arabia (within 3 yrs of travel)

- Age >2 yr 1 dose, Quadrivalent vaccine
- Age 3 m – 2 yr 2 doses, Men A containing vaccine

To endemic & hyperendemic area, during dry season

- 2 m – 55 yr quadrivalent (MCV)
- >55 yr quadrivalent (MPS)

MMWR 2013; 62:1-22
CDC Yellow Book 2016

ACIP References

- Yellow Fever - MMWR 2015; 64: 647-650
- Typhoid - MMWR 2015; 64: 305-308
- Hepatitis A - MMWR 2007; 56: 1080-1084
- Japanese Encephalitis - MMWR 2013; 62: 898-900
- Cholera – MMWR 2017; 66: 482-485
- Meningococcal - MMWR 2013; 62: 1-27

Safe Travel!